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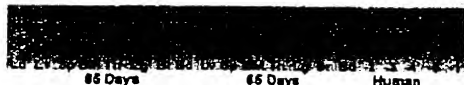
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DISTRIBUTION AND ENGRAFTMENT OF HUMAN MESENCHYMAL STEM CELLS (MSC) AFTER IN UTERO TRANSPLANTATION IN FETAL SHEEP. K.W. Liechty*, R. Milner*, A.F. Shaaban*, A.B. Mosley*, R. Deans*, M. Thiede*, A.W. Flake* (Intr. by E.D. Zanjan). *The Children's Institute for Surgical Science, The Children's Hospital of Philadelphia, Philadelphia, PA; Ostris Therapeutics, Inc. Baltimore, MD, USA.*

Mesenchymal stem cells (MSCs) are pluripotent cells of bone marrow origin. Under specific in vitro conditions, MSCs have the capacity to differentiate into osteoblasts, myoblasts, chondrocytes, adipocytes, or bone marrow stromal cells. Potential clinical applications of MSCs include cellular therapy, tissue engineering, and gene therapy. To assess the ability of human MSC to home and engraft in a known animal model of human hematopoiesis, we transplanted human MSCs by intravenous (I.v.) or intraperitoneal (i.p.) injection into 65 or 85 day gestation fetal sheep. Cell doses ranged from 5×10^6 MSC/fetus at 65 days gestation to 50×10^6 MSC/fetus at 85 days gestation. Recipients were sacrificed at 7 or 14 days after transplantation and the liver (Lv), spleen (Sp), bone marrow (BM), thymus (Th), lung (Lg), brain (Br), and blood (Bd) were analyzed by PCR for human specific β -2 microglobulin. Samples were compared to a dilutional curve of human DNA. The presence of human cells in PCR positive tissues was confirmed by immunohistochemistry.



Our findings demonstrate that human MSCs transplanted by either i.v. or i.p. routes can be detected by PCR and immunohistochemistry in many fetal tissues for at least 2 weeks following injection. A single 85 day animal has been sacrificed at 7 weeks after transplantation and PCR remains positive in the fetal liver. The significance of these findings for potential clinical application will be determined by long-term studies of persistence and differentiation of MSCs in the engrafted tissues.